III. REMARKS

Reconsideration of the present application as amended is respectfully requested.

A. Status Of The Claims

Claims 1-3, and 5-38 are pending in this application. Claims 4, and 39 to 41 have been cancelled without prejudice. Claims 14-18, 20, 27-28, 33, 34, and 38 have been amended without prejudice. It is respectfully submitted that no new matter has been added by virtue of this amendment.

B. Rejections under 35 U.S.C. § 112, Second Paragraph

In the Office Action, the Examiner rejected claims 16-18, 20, 27, 33 and 34 under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Specifically the Examiner states that "[t]he claims recite obtaining C_{max} or T_{max} values relative to the C_{max}/T_{max} provided by 'an immediate release hydrocodone reference formulation', [h]owever, the claim must recite the 'immediate release hydrocodone reference formulation' which is critical to apprise one of ordinary skill in the art to determine what C_{max}/T_{max} values are within the metes and bounds of the claim; since varying the 'immediate release hydrocodone reference formulation' will vary the presently claimed C_{max}/T_{max} parameters.

In response, Applicants have amended the claims without prejudice to include the term "Lortab®". Support for the inclusion of Lortab® can be found at page 8, lines 16 to 19. It is respectfully submitted that one of ordinary skill would understand Lortab® to be representative of the hydrocodone/acetaminophen combination tablet, commercially available from UCB Pharma, Inc, on the day that the present application was filed.

In view of the amendments made and arguments presented, withdrawal of the Examiner's 35 U.S.C. § 112, second paragraph rejection of claims 16-18, 20, 27, 33 and 34 is respectfully requested.

C. **Rejections under 35 U.S.C. § 102 and § 103**

In the Office Action, the Examiner rejected claims 1-3 and 5-41 under 35 U.S.C. § 102(a,b,e) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,639,476 to Oshlack et al. (hereinafter "Oshlack et al."). In the rejection, the Examiner notes that "the presently claimed compositions result in *various pharmacologic parameters*," and lists certain parameters in the claims. The Examiner further notes that Oshlack et al. teaches controlled release oral dosage forms, and "[t]eaching of opioid as the most preferred active agent (e.g., see examples and patent claims) with the preferred opioid analgesics comprising less than 15 members, one of which is hydrocodone (e.g., see paten[t] claim 6) . . . ." The Examiner further states that the "Oshlack et al. reference compositions further discloses controlled release profiles; alterable by changing resin concentrations; and methods of manufacture which are clearly within the scope of the presently claimed invention." (Citations omitted). The Examiner concludes that "the Oshlack et al. reference anticipates or alternatively renders obvious compositions (and methods of making and use) within the scope of the presently claimed invention; in which the resulting compositions MUST *inherently* possess *the various pharmacologic parameters* as presently claimed." (Citations omitted).

This rejection is traversed. Initially, it is noted that Oshlack et al. disclose certain pharmacokinetic parameters with respect to dosage forms containing hydromorphone or morphine as the active agent. However, Oshlack et al. fail in the very least to teach, hint or suggest any pharmacokinetic parameters with respect to dosage forms containing hydrocodone or a pharmaceutically acceptable salt thereof as recited in the present claims.

Further, claims 1, 32, 36, 37, and 38 recite an oral dosage form comprising hydrocodone or a pharmaceutically acceptable salt thereof, suitable for twice-a-day administration to a human patient, said dosage form after a first administration to a human patient, providing a C_{12}/C_{max} ratio of 0.55 to 0.85. Oshlack et al. fail in the very least to teach, hint or suggest a dosage form comprising hydrocodone or a pharmaceutically acceptable salt thereof suitable for twice a day

administration providing such a C_{12}/C_{max} ratio. In addition, even assuming arguendo that one of ordinary skill would attempt to calculate a C_{12}/C_{max} ratio for the pharmacokinetic parameters disclosed in Oshlack et al. with respect to opioid formulations exemplified in Oshlack et al., it is respectfully submitted that one of ordinary skill in the art would look to Table 26 of Examples 19-20 which includes MS Contin®, a known 12 hour opioid formulation suitable for twice a day administration. As the present claims recite a dosage form suitable for twice a day administration, it is respectfully submitted that MS Contin® is the only formulation described in the Examples of Oshlack et al. which could be related to the formulations of the present invention. However, according to Oshlack et al. the specified C_{12}/C_{max} ratio as recited in the present claims is not achieved by such MS Contin® formulations.

For example, in Examples 19-20 of Oshlack et al. a bioavailability study was conducted using formulations of Example 19, 20 and MS Contin® 30 mg (Example 19A) as a reference. The results set forth in Table 26 indicate that MS Contin® has a Cmax of 11.6 ng/ml. Figure 8 of Oshlack et al. indicates the plasma levels of Example 19A (MS Contin®), and at the 12 hour time point in Figure 8, the plasma concentration is about 1.8 ng/ml for Example 19A. The calculated C_{12}/C_{max} ratio is $1.8/11.6 = 0.16$, which does not fall within the ratio recited in the present claims.

Therefore, in view of the above, Oshlack et al. fail to teach, hint or suggest twice-a-day formulations having the C_{12}/C_{max} ratios as recited in the present claims.

In addition, Oshlack et al. fail to teach, hint or suggest providing dosage form comprising hydrocodone or a pharmaceutically acceptable salt thereof suitable for twice a day administration which provides "a rate of absorption during the time period from T_{max} to about 12 hours after oral administration of the dosage form which is from about 55% to about 85% of the rate of elimination during the same time period" as recited in claim 31; which provides "a mean C_{max} of hydrocodone which is less than about 50% of the C_{max} of an equivalent dosage for an immediate release hydrocodone reference formulation under the trademark Lortab® as recited in claim 33; which provides "a time to 80% mean C_{max} which is about 90% to about 110% of the time to 80%

mean C_{max} of an equivalent dose of an immediate release hydrocodone reference formulation under the trademark Lortab® as recited in claim 34; or which provides a mean in-vivo absorption rate from the time of oral administration to a human patient to T_{max} of about 2 mg/hour to about 4 mg/hour and which provides a mean in-vivo absorption rate from T_{max} to about 12 hours after administration which is from about 0.08 mg/hour to about 0.4 mg/hour, said dosage form providing a therapeutic effect for at least 12 hours, based on oral administration of a dosage form containing 15 mg hydrocodone bitratrate as recited in claim 35; as Oshlack et al. provide no such teaching with respect to hydrocodone or a pharmaceutically acceptable salt thereof.

In view of the aforementioned remarks, withdrawal of the Examiner's 35 U.S.C. § 102 (a, b, e) and 35 U.S.C. § 103(a), rejections of claims 1-3, 5-41 is respectfully requested.

D. Conclusion

In view of the actions taken, it is respectfully submitted that this application is now in condition for allowance.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,
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